PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants:	Wesley Blackaby, et al.		
Serial No.:	10/593,950	Case: 21573YP	Art Unit: 1614
Filed:	May 10, 2007		
For:	HETEROARYL PIPERIDINE GLYCINE TRANSPORTER INHIBITORS		Examiner: Ricci, Craig D.

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

DECLARATION OF SCOTT WOLKENBERG

Sir:

I, Scott Wolkenberg, hereby declare the following:

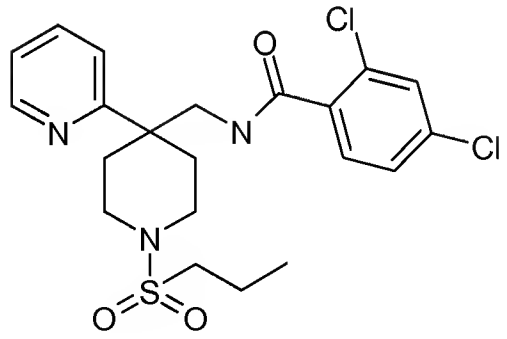
1. I have been employed by Merck & Co., Inc. beginning in 2003 and currently hold the title of Research Fellow in the Department of Medicinal Chemistry.

2. I am a joint inventor in the above-referenced patent application and have read the Office action mailed December 23, 2008 issued therein.

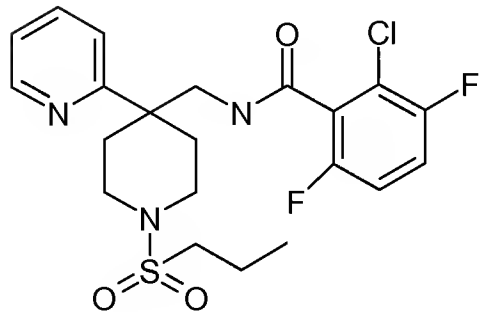
3. My job responsibilities at Merck included synthesizing compounds that were inhibitors of the glycine transporter GlyT1 and managing other chemists in synthesizing compounds for this target. As part of our efforts in this research, we routinely had the synthesized compounds tested in various *in vitro* and *in vivo* assays predictive of drug efficacy and safety.

4. As part of the research efforts described above, the following 4-pyridylpiperidine and 4-phenylpiperdine GlyT1 inhibitors were tested in the Preincubation Time Dependent Inhibition of CYP3A4 in Human Liver Microsomes assay described in the following references: Silverman RB 1995. Mechanism-Based Enzyme Inhibitors. *Enzyme Kinetics and Mechanism*, Pt D 249:240-283; Brown HS, Ito K, Galetin A, Houston JB 2005. Prediction of in vivo drug-drug interactions from in vitro data: impact of incorporating parallel pathways of drug elimination and inhibitor absorption rate constant. *Br J Clin Pharmacol* 60:508-518; and Wang YH, Jones DR, Hall SD 2004. Prediction of cytochrome P450 3A inhibition by verapamil enantiomers and their metabolites. *Drug Metab Dispos* 32:259-266. Time dependent inhibition of CYP3A4 can be predictive of clinically significant drug-drug interactions. Next to each compound below is an indication whether the compound tested positive (defined as >50% loss of activity versus control) or negative (<50% loss of activity vs control) in this *in vitro* assay.

4-pyridylpiperidines:



TDI –



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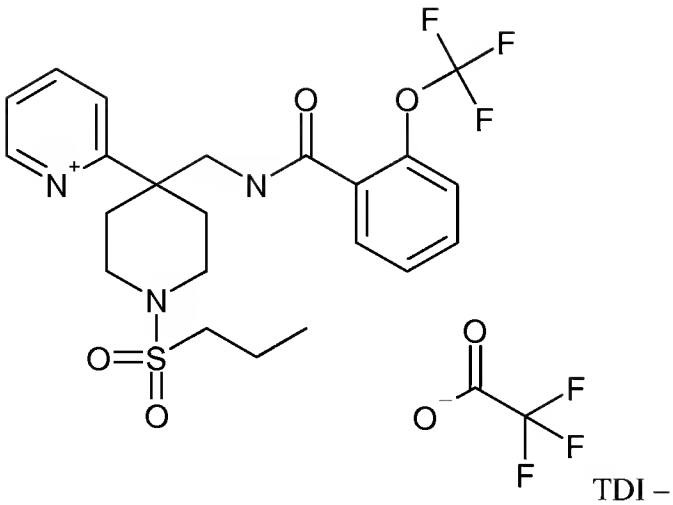

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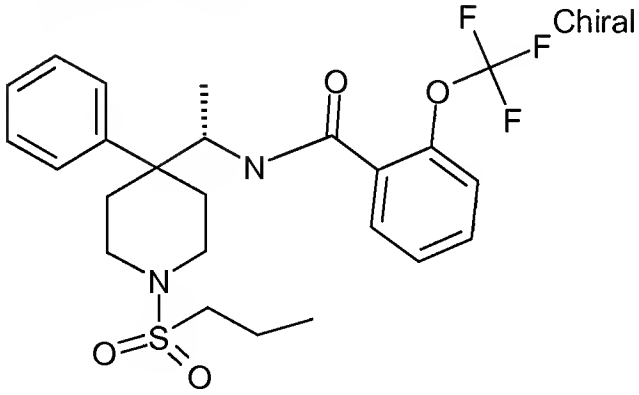
4-phenylpiperidines:



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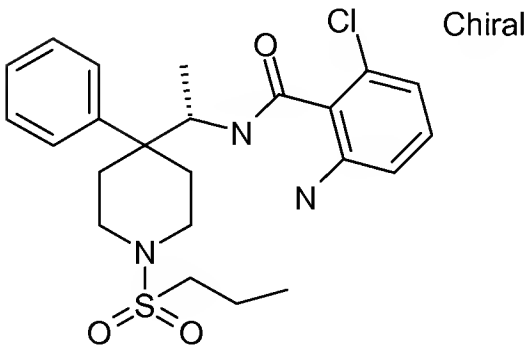

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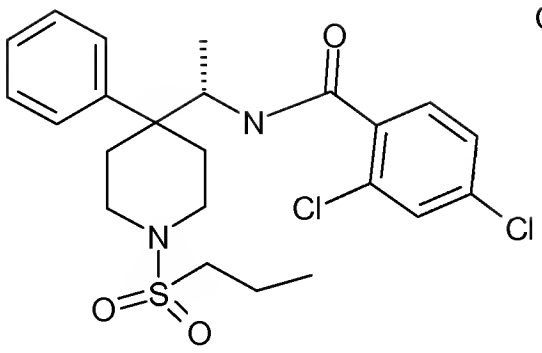

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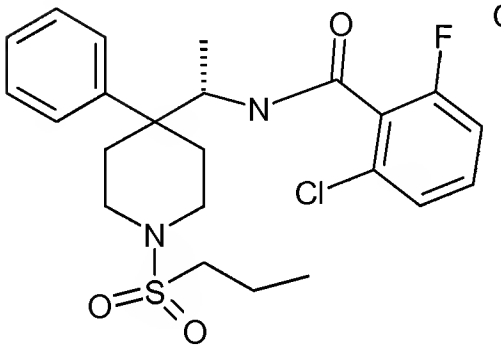

TDI +

5. I hereby declare that all statements made herein of my own knowledge are true and that all statement made of information and belief are believed to be true and further that these statements are made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Respectfully submitted,

By /Scott E. Wolkenberg/
Scott E. Wolkenberg

Date: March 23, 2009